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Original Paper

The Importance of a Multidisciplinary Group in the Treatment of Soft Tissue Sarcomas

T. Wiklund,[1] R. Huuhtanen,[1] C. Blomqvist,[1] E. Tukiainen,[2] M. Virolainen,[1] P. Virkkunen,[1] S. Asko-Seljavaara,[2] J.M. Björkenheim[3] and I. Elomaa[1]

[1]Department of Radiotherapy and Oncology; [2]Department of Plastic Surgery; and [3]Department of Orthopaedics and Traumatology, Helsinki University Hospital, FIN-00290 Helsinki, Finland

In 1987, a multidisciplinary soft tissue sarcoma (STS) group was established and a treatment protocol was set up. By 1993, there were 193 patients with a diagnosis of STS of the superficial trunk or extremities. 134 patients were referred with primary (stage M0) tumours and treated with curative or palliative intention. Nine amputations were performed. 94 (70%) patients were treated with wide or compartment surgery ($n = 62$) or marginal surgery combined with postoperative radiotherapy ($n = 32$). According to the protocol, these patients had received adequate treatment. 18 patients have recurred locally (13%) (median follow-up: 36 months). 12 were salvaged. 33 had metastases. The estimated 3-year survival, local control and disease-free survival rates are 79, 87 and 69%, respectively. These results compare favourably with previously published results from this hospital and from a nationwide study. The improved results emphasise the importance of a multidisciplinary STS group.

Key words: combined-modality therapy, sarcoma-surgery, sarcoma-radiotherapy
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INTRODUCTION

THE MAIN measurements of outcome in the treatment of soft tissue sarcomas (STS) are survival, local control and function. The impact of local control on survival has been questioned [1–3]. However, local control is important both from a psychological and functional point of view. The growing stress on functional outcome has also emphasised the aim of performing limb sparing surgery. Thus, radiotherapy has been increasingly used as an adjunct to surgery [4–6]. This multidisciplinary approach has led to the foundation of sarcoma groups at major cancer centres [7, 8]. This intuitively natural development lacks formal justification.

In Helsinki University Hospital, Finland, an STS group was established in 1987. This group consists of oncologists, radiotherapists, orthopaedic surgeons, plastic surgeons, pathologists and radiologists. The group meets weekly, and new cases are discussed before treatment. Postoperatively, the patients are rediscussed and decisions are made on further treatment.

We now report the results on the patients referred to this group, and the results are compared with those reported from this hospital and the whole of Finland during recent decades in an attempt to evaluate whether the foundation of a sarcoma multidisciplinary team has led to a significant improvement in the treatment results.

Correspondence to T. Wiklund.
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PATIENTS AND METHODS

The sarcoma group was established in August 1987. Based on current literature, a treatment protocol was set up. The protocol emphasised limb sparing surgery and recommended postoperative radiotherapy after marginal surgery. Reconstructive surgery was encouraged.

Pre-operatively, the tumour was imaged by computed tomography and/or magnetic resonance imaging (1.0 T), and ultrasound. Fine needle aspiration and histological core biopsies were taken by means of ultrasound targeting. To avoid contamination with tumour cells, the biopsy track was placed in such a way that it could be excised with the specimen at the time of definite surgery. For high grade malignancy, a computed tomography of the lungs was performed.

The surgical margins were analysed by the pathologist, the surgeon and the radiation oncologist based on gross and microscopic findings. The surgical margins were defined as

compartmental if an intracompartmental tumour, and the whole muscle-compartment were excised en bloc including the natural barriers of the compartment. The margin was defined as wide if the tumour was excised with a macroscopic margin of at least 5 cm (or at least 2.5 cm microscopically). However, a smaller margin was accepted if it consisted of an uninvolved natural anatomical barrier (e.g. fascia). If the requirements for a wide margin were not fulfilled, the margin was classified as marginal (margins less than wide and only microscopic residual) or intralesional (macroscopic tumour left).

The primary treatment was surgical resection in all cases where the tumour could be removed without major sacrifice of function. If the pre-operative investigations indicated that adequate surgical margins were not achievable, surgery was aimed at marginal surgical margins. For intralesional surgery, re-operation was recommended.

Amputation was recommended for extensive infiltration of a major nerve, of vascular structures, or of a joint or bone so that even marginal resection was not feasible, or if limb sparing surgery would lead to significant shortening of the limb, or for local recurrence after radiotherapy or progression during radiotherapy.

Radiotherapy was recommended after marginal surgery. If a re-operation was not technically feasible after marginal or intralesional surgery, radiotherapy was recommended. Post-operative radiotherapy was preferred. During recent years, pre-operative radiotherapy was recommended in cases considered for amputation, especially if marginal surgical margins were not expected to be achieved.

The radiotherapy was, in general, delivered through two opposed individually formed fields. Treatment planning was based on computed tomography. Patients with extremity tumours were individually fixated. The target volume was defined as the involved muscle compartment in the transversal direction, and a margin of at least 5 cm longitudinally. A strip of subcutis was spared as well as a part of a long bone or joint when feasible. The radiation dose was 50 Gy in 5 weeks (2 Gy/day). For microscopically positive surgical margins, a boost was delivered to a smaller target volume (10–20 Gy in 1–2 weeks).

Adjuvant chemotherapy was not routinely used, except for extraskeletal Ewing's sarcomas and related tumours.

Adequate treatment was defined as wide or compartmental surgery alone or marginal surgery combined with radiotherapy.

The patients were followed-up regularly. For high grade sarcomas, the interval was 2 months during the first 2 years, thereafter 2–3 times yearly. A chest X-ray was taken at each visit. Computed tomography scans from the operative area were taken 6 months postoperatively and thereafter if indicated. Low grade tumours were followed 2–3 times yearly.

Pulmonary metastases were surgically excised whenever feasible. For inoperable metastatic disease, combination chemotherapy was used, combined if there was a favourable response with local therapy (surgery or radiotherapy).

Statistical methods

The overall, metastases-free, disease-free, and local recurrence-free survival were calculated with Kaplan–Meier analysis. Differences between the survival of different subgroups were analysed with the Mantel–Cox test. In the multivariate analysis, the proportional hazards method was used. In this analysis, size was a continuous variable.

RESULTS

A total of 452 patients were referred to the group between August 1987 and May 1993. 193 patients had a final diagnosis of STS of the superficial trunk or the extremities. 46 of these patients were referred for locally recurrent tumours, with or without metastatic disease. Thus, 147 patients were referred for a primary STS of the superficial trunk or the extremities. 12 patients had haematogenous metastases at diagnosis and 1 patient refused any therapy, and were excluded from the analysis. This report concerns 134 patients with a primary STS of the trunk ($n = 30$) or the extremities ($n = 104$), who had no metastases at time of diagnosis and received treatment. Half the patients were referred after marginal surgery (51%), 25% either after fine needle aspiration biopsy or left untouched.

The mean age of the 134 patients was 51 years (range 16–91 years). 61 (46%) were males. The performance status was WHO 0–1 in 94% of the patients. In 1 case the tumour was a postirradiation sarcoma, two tumours developed in areas of chronic infection/inflammation and 4 patients had Recklinghausen's disease.

The histological types are described in Table 1. Characteristics of the tumours are shown in Table 2. The median tumour size was 5 cm (mean 6.8, range 0.6–25 cm). 2 patients had cytologically verified lymph node metastases.

Limb-sparing surgery was achieved in 95 (91%) patients with tumours of the extremities or the limb girdles.

With a median follow-up time of 36 months (mean 37.8, range 3.4–81.7 months), the estimated local control rate at 3 years was 87%. The local control rates in groups with different tumour characteristics and therapy are shown in Tables 2 and 3. The local control is also described in Figure 1. Of patients with tumours of the limbs and the limb girdles, the estimated 3 year local control rate was 88%.

30 patients were treated with inadequate surgery only. The most common reason for the decision not to give postoperative radiotherapy was low malignancy grade, with an expected low risk for local recurrence (18 patients). Other reasons for a decision of marginal surgery without radiotherapy were high age, poor general condition, and refusal of further therapy. The estimated rate of local recurrence at 3 years among patients who had a marginal surgical margin without radiotherapy was 15% and 33% in low grade and high grade tumours, respectively.

The records of the patients with local recurrence were re-

Table 1. Histological types of 134 soft tissue sarcomas of the extremities and the trunk

Malignant fibrous histiocytoma	31	(23%)
Leiomyosarcoma	22	(16%)
Liposarcoma	14	(10%)
Dermatofibrosarcoma protuberans	11	(8%)
Synovial sarcoma	8	(6%)
Extraskeletal Ewing's sarcoma	8	(6%)
Malignant Schwannoma	5	(4%)
Fibrosarcoma	6	(4%)
Other specified	13	(10%)
Not specified	16	(12%)

Table 2. Description of tumour characteristics in the study population, and the corresponding estimates of 3-year local control rates

Tumour characteristics	No. of patients (%)	Estimated 3 years local control
Site		
Lower extremity	72 (54%)	89%
Upper extremity	32 (24%)	87%
Trunk	30 (22%)	83%
Grade		
Low	51 (38%)	91%
High	83 (62%)	85%
Depth		
Cutaneous	3 (2%)	93%
Subcutaneous*	56 (42%)	
Intramuscular	7 (5%)	100%
Extramuscular†	68 (51%)	81%
Compartment		
Intracompartmental	13 (10%)	100%
Extracompartmental‡	79 (59%)	88%
Unclassified	42 (31%)	82%
Size§		
< 5 cm	55 (41%)	95%
5–10 cm	43 (32%)	83%
> 10 cm	35 (26%)	84%

* Subcutaneous tumours with or without cutaneous extention but without involvement of the deep muscle fascia. † Extramuscular tumours, intramuscular tumours with extramuscular extention or tumours penetrating the deep fascia either from the subcutis or vice versa. ‡ Subcutaneous tumours were not classified. § Data for 1 patient was missing.

Table 3. Local recurrence by treatment category

Surgical margin and radiotherapy	Inadequate treatment No. of patients/ (no. of local failures)/ estimated 3 year local control*	Adequate treatment No. of patients/ (no. of local failures)/ estimated 3 years local control*
No surgery + RT	1 / (0)	
Intralesional + RT	9 / (3) / 66%	
Marginal – RT	30 / (7) / 78%	
Marginal + RT		32 / (4) / 86%
Wide (one + RT)		60 / (3) / 95%
Compartmental (one + RT)		2 / (1)
Total	40 / (10) / 76%	94 / (8) / 92%

RT, radiotherapy. *Kaplan–Meier.

analysed in detail by the entire group. A description of the patients with local recurrence is given in Table 4. Of note is that 8 patients had metastases before or at the time of local recurrence. This was the case in all 3 patients with an intralesional surgical margin and local recurrence. A further 3 patients had subsequent metastases. Furthermore, 12 patients achieved local control with salvage treatment. Of 5 patients with local recurrence within the radiation treatment volume,

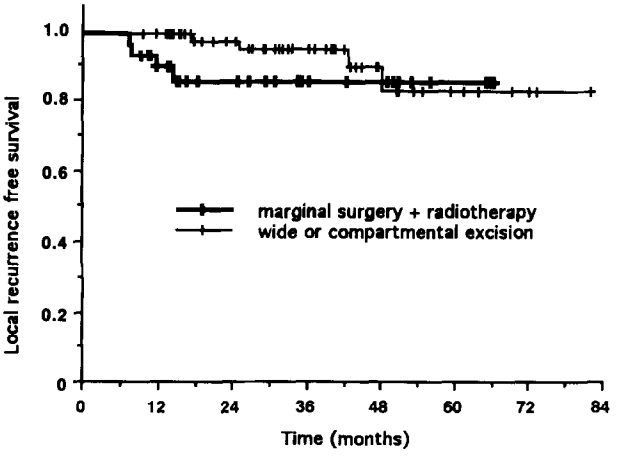

Figure 1. Local recurrence-free survival of patients treated with marginal surgery and postoperative radiotherapy and patients treated with wide or compartmental surgery (in 2 cases followed by radiotherapy).

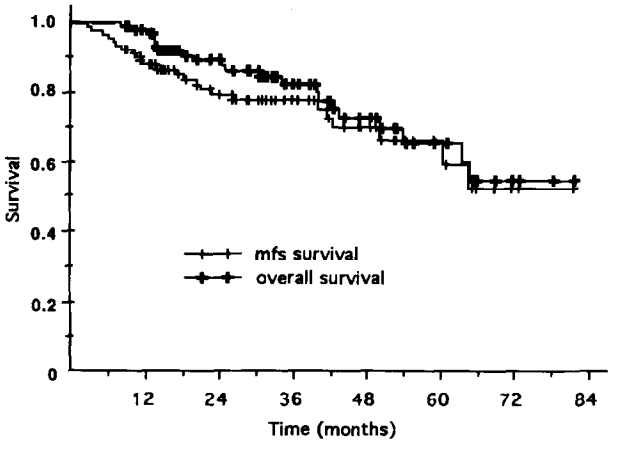

Figure 2. Metastases-free and overall survival of all the 134 patients included in the analysis.

3 had intralesional surgery (i.e. macroscopic tumour at start of radiotherapy). 3 patients had the recurrence at the border of the radiation treatment volume. Of these, 1 could not be optimally treated for a postirradiation sarcoma due to a high previous normal tissue exposure to radiation. Another patient had a sarcoma of her breast. Pre-operatively she was judged to have mammary cancer and the axillary nodes were removed. The radiotherapy was delivered only to the thoracic wall, not to the axillary region. The subsequent recurrence was in the axilla. 2 patients had recurrence within the same limb (1 within the radiation volume, the other at the radiation volume border), but in an untouched compartment or area. These were classified as local recurrence. The treatment protocol was clearly not followed in 4 of the patients who had a local recurrence (1 refused further treatment, in 1 case the local hospital did not deliver the suggested treatment and accepted an increased risk for local recurrence, in 1 case the treatment was aimed at palliation due to the high age of the patient, and finally in 1 case the diagnosis was wrongly benign). In a further 2 patients, the definitions of surgical margins were not followed, and the margins were reclassified to marginal. Finally, in 2 patients the initial work-up and surgery were

Table 4. Characteristics of patients who have had local failure

Surgical margin	Macro/microscopic margin (in cm)	Radiotherapy	Metastases before or at time of local recurrence	Metastases during subsequent follow-up	Subsequent follow-up months, status	Local control at last follow-up	Comments
Marginal + contamination	0/0	No	Yes	Yes	13, DOD	No	Non-radical treatment accepted
Marginal	2.5/2.5	No	No	Yes	11, ALIVE MET	Yes	Non-radical treatment accepted
Marginal	—/—	No	No	No	26, ALIVE NED	Yes	Non-radical treatment accepted
Marginal	0/0	No	No	No	28, ALIVE NED	Yes	Inadequate postoperative evaluation
Marginal	—/—	No	No	No	5, ALIVE NED	Yes	Non-radical treatment accepted
Marginal	2/—	No	No	No	11, ALIVE NED	Yes	Inadequate treatment
Marginal	1.75/1.75	No	No	No	8, ALIVE NED	Yes	Inadequate pre-operative evaluation, surgical miss
Wide	—/—	No	Yes	Yes	8, DOD	No	Inadequate postoperative evaluation
Wide	5/—	No	No	Yes	41, ALIVE NED	Yes	Adequate treatment
Wide	—/—	No	No	No	2, ALIVE NED	Yes	Multiple surgery, probably contamination
Intralesional	0/0	Yes	Yes	Yes	9, DOD	Yes	In-field recurrence
Intralesional	0/—	Yes	Yes	Yes	19, ALIVE MET	No	In-field recurrence
Intralesional	0/—	Yes	Yes	Yes	13, ALIVE MET	Yes	In-field recurrence
Marginal	1.5/—	Yes	No	Yes	4, DOD	Yes	In-field recurrence
Marginal	0.4/0.3	Yes	No	No	10, ALIVE LOC REC	No	Border recurrence
Marginal	< 1/—	Yes	Yes	Yes	1, DOD	No	Border recurrence
Compartmental	—/—	Yes	Yes	Yes	10, ALIVE MET	No	In-field recurrence
Marginal amputation	2/1	Yes	Yes	Yes	8, DOD	Yes	Border recurrence

DOD, dead from sarcoma; ALIVE MET, alive with metastatic disease; NED, no evidence of disease; ALIVE LOC REC, alive with local recurrence.

inadequate and led to surgical location miss and repetitive surgery.

33 patients have had metastases during the follow-up (25%). In patients with high grade tumours, the estimated rate of metastases-free survival at 3 years was 61%, and in those with low grade tumours 97%. The estimated disease-free, metastases-free and overall survival rates at 3 years were 69, 74 and 79%, respectively (Figure 2).

Four amputations have been performed for local recurrence or complications. Thus, the final rate of amputations in 104 patients with extremity and limb girdle tumours was 12%.

Factors affecting local recurrence in Cox analysis on time to local recurrence were adequacy of treatment (adequate treatment versus other treatment, $P = 0.02$) and depth of the tumour (cutaneous, subcutaneous, and intramuscular versus extramuscular, $P = 0.01$). Factors without statistically significant impact on local recurrence-free survival were site (extremity versus trunk), histological grade (high versus low),

and size. In the stepwise regression analysis, the only factor which retained significance was depth of the tumour. After exclusion of this factor, adequacy of treatment still approached statistical significance ($P = 0.053$).

DISCUSSION

The importance of specialised sarcoma groups has repeatedly been stressed [7, 8]. We were encouraged to start a multimodality STS group in 1987. First we decided on a treatment protocol. In this study, we present how well this protocol was followed and the impact of this work on local control and the rate of amputations.

The treatment protocol turned out to be appropriate. A similar protocol has also recently been reported by others [5]. Local control was acceptable and the number of amputations was small. However, it should be emphasised that the material was not population based. Thus, extracompartmental, extramuscular and large tumours were overrepresented [9]. It is assumed that small subcutaneous tumours which did not need reconstructive surgery and intramuscular tumours were treated at local hospitals. This is also suggested by the high proportion of patients referred after marginal surgery. In population based series, local control has been excellent in intramuscular and subcutaneous tumours with surgery alone [9].

A significant improvement has taken place compared to previously published results from this hospital and population-based Finnish material [10, 11]. In the population-based material by Rantakokko and Ekfors, 48% of the patients with extremity STS treated between 1960 and 69 in Finland had local recurrence [11]. In a previous report from this hospital, the 3-year disease-free survival was only 36% in patients treated between 1965 and 1975 [10]. The rate of amputations was 10% in the population-based study [11]. Established STS groups have recently reported results similar to ours. In Southern Sweden, the local recurrence rate was 11% in nearly population-based material [9], whereas the specialised team from the Roswell Park Memorial Institute has reported a 6% local recurrence rate in patients treated either with a wide resection alone or a marginal resection combined with postoperative radiotherapy [5].

The relatively high local recurrence rate in patients with protocol deviations for various clinical reasons indicate that the strict adherence to the treatment protocol might yield better results than individualised treatment. In some patients, inadequate treatment was accepted due to patient selection, selection of local doctors or the sarcoma group (i.e. high age, poor general condition, etc.). The most common identified reason for protocol deviation was omission of radiotherapy after marginal surgery for low grade sarcomas. Radiotherapy should probably be applied after marginal surgery independently of histological grade.

Recurrence after intralesional surgery was noted in 3 of the 9 patients, even after high dose postoperative radiotherapy. In these patients, the appropriate rationale would probably have been pre-operative radiotherapy followed by surgery or amputation. After marginal surgery, recurrence within the radiation field was uncommon.

All patients with local failure were thoroughly evaluated by the group. In many cases, the cause for local recurrence seemed evident in retrospect. In several cases, the patients were referred after inadequate pre-operative radiological work-up and inadequate surgery, thus precluding precise localisation of the area at risk. The question was also raised how to define a local recurrence. One patient had a recurrence within the same extremity as the primary tumour but in an untouched compartment at time of widespread metastatic disease including soft tissue metastases.

Local recurrence was in many cases of minor clinical importance. Many of the patients had metastases preceding the local relapse. The patients most often die from metastases, rarely from local failure. Moreover, the majority of the locally recurrent tumours were salvaged. Local recurrence in patients with limb sarcomas must therefore be weighed against the benefit of the spared limb, and although local failure undoubtedly is a psychological stress for the patient, an increased risk for local failure may be acceptable in the individual patient.

In conclusion, these results indicate that a sarcoma group can readily be started, and that it is possible to follow our protocol. A multimodality group is, however, costly and resource-demanding. This hospital is the central hospital for approximately 1.5 million inhabitants. Currently, we treat approximately 2 new patients with STS weekly. In addition, about the same number of patients with benign tumours are referred weekly. Thus, we handle approximately 8–10 cases at our weekly meetings. This is probably close to the minimum number of patients to justify a group with weekly meetings.

1. Emrich LJ, Ruka W, Driscoll DL, Karakousis CP. The effect of local recurrence on survival time in adult high-grade soft tissue sarcomas. *J Clin Epidemiol* 1989, **42**, 105–110.
2. Stotter AT, A'Hern RP, Fisher C, Mott AF, Fallowfield ME, Westbury G. The influence of local recurrence of extremity soft tissue sarcoma on metastasis and survival. *Cancer* 1990, **65**, 1119–1129.
3. Barr LC, Stotter AT, A'Hern RP. Influence of local recurrence on survival: a controversy reviewed from the perspective of soft tissue sarcoma. *Br J Surg* 1991, **78**, 648–650.
4. Brennan MF, Hilaris B, Shiu MH, *et al.* Local recurrence in adult soft-tissue sarcoma. *Arch Surg* 1987, **122**, 1289–1293.
5. Karakousis CP, Emrich LJ, Rao U, Khalil M. Limb salvage in soft tissue sarcomas with selective combination of modalities. *Eur J Surg Oncol* 1991, **17**, 71–80.
6. Suit HD, Mankin HJ, Wood WC, *et al.* Treatment of the patient with stage M0 soft tissue sarcoma. *J Clin Oncol* 1988, **6**, 854–862.
7. Brennan MF, Casper ES, Harrison LB, Shiu MS, Gaynor J, Hajdu SI. The role of multimodality therapy for soft-tissue sarcoma. *Ann Surg* 1991, **214**, 328–338.
8. Suit HD. The George Edelstyn memorial lecture: radiation in the management of malignant soft tissue tumours. *Clin Oncol R Coll Radiol* 1989, **1**, 5–10.
9. Rydholm A, Gustafson P, Rööser B, *et al.* Limb-sparing surgery without radiotherapy based on anatomic location of soft tissue sarcoma. *J Clin Oncol* 1991, **9**, 1757–1765.
10. Gröhn P, Heinonen E, Santavirta S, Sandelin J, Sundell B, Holsti LR. The management of soft tissue sarcomas. *Duodecim* 1979, **95**, 1301–1306.
11. Rantakokko V, Ekfors TO. Sarcomas of the soft tissues in the extremities and limb girdles. Analysis of 240 cases diagnosed in Finland in 1960–1969. *Acta Chir Scand* 1979, **145**, 385–394.

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